

**AMENDMENT**

Kindly amend the specification, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, as follows.

**IN THE CLAIMS:**

Kindly amend the claims, without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents, to read as follows:

1. (Previously presented) A device for forming and/or increasing the relative number of undifferentiated cells in a cell population including committed cells, which device comprises a chamber, means for introducing into said chamber a cell population including committed cells, means for introducing into said chamber an agent capable of increasing the relative number of undifferentiated cells in a cell population, incubation means for incubating said committed cells in the presence of said agent, and mixing means for mixing the agent and the cell population in the chamber.

2. (Previously presented) A device for forming and/or increasing the relative number of undifferentiated cells in a cell population including committed cells, which device comprises a chamber, means for introducing into said chamber a cell population including committed cells, means for introducing into said chamber an agent capable of increasing the relative number of undifferentiated cells in a cell population,, and incubation means for incubating said agent and said committed cells, and mixing means for mixing the agent and the cell population in the chamber.

3. (Original) A device according to claim 1 wherein said device comprises:  
measuring means for measuring the volume of said cell population; and/or  
means for conducting cell counts and for measuring the cell concentration of said cell population; and/or  
transfer means for transferring an amount of said cell population from a storage container to said chamber; and/or

transfer means for transferring a pre-determined amount of said cell population from a storage container to said chamber; and/or

calculator means for calculating the volume of agent to be added to the chamber; and/or

transfer means for transferring a volume of agent to the chamber; and/or

transfer means for transferring a calculated volume of agent to the chamber; and/or

carbon dioxide control means for controlling the concentration of carbon dioxide in said chamber; and/or

temperature control means for controlling the temperature in said chamber; and/or

mixing means for mixing the cell population and agent within the chamber; and/or

timing means for timing the incubation period; and/or

display means for displaying to the user the remaining time period of the incubation period; and/or

alarm means for alerting the user of completion of the incubation period; and/or

harvesting means for harvesting cells from the chamber; and/or

removal means for removing a sample of cells, comprising undifferentiated cells, from the chamber into a storage container; and/or

sealing means for sealing a storage container comprising a population of cells comprising undifferentiated cells; and/or

communicating means for the device to remotely communicate orders and/or confirm that operations are being or have been performed correctly.

4. (Canceled)

5. (Original) A device according to claim 3 wherein the means for conducting cell counts is a coulter counter.

6. (Canceled)

7. (Original) A device according to claim 3 wherein the means for conducting cell counts is a cytometer.

8-10. (Canceled)

11. (Original) A device according to claim 3 wherein said transfer means for transferring a volume of agent to the chamber is a syringe driven by a motor.

12. (Canceled)

13. (Original) A device according to claim 3 wherein said transfer means for transferring a calculated volume of agent to the chamber is a syringe driven by a motor.

14. (Canceled)

15. (Original) A device according to claim 3 wherein the harvesting means harvests the undifferentiated cells from the chamber.

16. (Canceled)

17. (Previously presented) A device according to claim 3 wherein the communicating means includes a microprocessor to collect and/or store data pertaining to agent(s) increasing the relative number of undifferentiated cells in a cell population, and/or ordering a supply thereof and/or operations and modem means for transmitting such data.

18. (Canceled)

19. (Currently amended) A device according to any one of claims 1-3[[4]] wherein the committed cells are non-cancer cells.

20. (Currently amended) A device according to any one of claims 1-3[[4]] wherein the committed cells are differentiated cells.

21. (Currently amended) A device according to any one of claims 1-3[[4]] wherein the committed cells are committed haematopoietic cells.

22. (Currently amended) A device according to any one of claims 1-3[[4]] wherein the committed cells are selected from CFC-T cells, CFC-B cells, CFC-Eosin cells, CFC-Bas cells, CFC-GM cells, CFC-MEG cells, CFC-E cells, T cells and B cells.

23. (Currently amended) A device according to any one of claims 1-3[[4]] wherein the undifferentiated cells are pluripotent stem cells.

24. (Currently amended) A device according to any one of claims 1-3[[4]] wherein the undifferentiated cells are stem cells selected from the group consisting of haematopoietic stem cells, neuronal stem cells, epithelial stem cells, mesenchymal stem cells, endodermal stem cells and embryonic stem cells.

25. (Currently amended) A device according to any one of claims 1-3[[4]] wherein the undifferentiated cells are characterised by one or more of the following cell surface marker designations: CD34+, HLA-DR-, CD38-, CD117, AC133, CD90 and/or CD45<sup>low</sup>.

26. (Currently amended) A device according to any one of claims 1-3[[4]] wherein the undifferentiated cells are MHC class I+ and/or MHC class II+ cells.

27. (Currently amended) A device according to ~~any one of claim~~[[s]] 2 [[or 4]] wherein the agent engages a receptor that mediates capture, recognition or presentation of an antigen at the surface of the committed cells.

28. (Original) A device according to claim 27 wherein the receptor is an MHC class I antigen or an MHC class II antigen.

29. (Original) A device according to claim 28 wherein the class I antigen is an HLA-A receptor, an HLA-B receptor, an HLA-C receptor, an HLA-E receptor, an HLA-F receptor or an HLA-G receptor and said class II antigen is an HLA-DM receptor, an HLA-DP receptor, an HLA-DQ receptor or and HLA-DR receptor.

30. (Original) A device according to claim 29 wherein the receptor is an HLA-DR receptor.

31. (Original) A device according to claim 27 wherein the receptor comprises a  $\beta$ -chain having homologous regions.

32. (Original) A device according to claim 31 wherein the receptor comprises at least the homologous regions of the  $\beta$ -chain of HLA-DR.

33. (Original) A device according to claim 27 wherein the agent is an antibody to the receptor.

34. (Original) A device according to claim 33 wherein the agent is a monoclonal antibody to the receptor.

35. (Original) A device according to claim 33 wherein the antibody is selected from the group consisting of monoclonal antibody CR3/43 and the monoclonal antibody TAL 1B5.

36. (Original) A device according to claim 34 wherein the antibody is selected from the group consisting of monoclonal antibody CR3/43 and the monoclonal antibody TAL 1B5.

37. (Original) A device according to any one of claims 2 or 4 wherein the agent modulates MHC gene expression.

38. (Original) A device according to claim 37 wherein the agent modulates MHC class I+ and/or MHC class II+ expression.

39. (Original) A device according to any one of claims 1-4 wherein the cell population including committed cells is a buffy coat blood sample or is from a buffy coat blood sample.

40. (Previously presented) A device for forming and/or increasing the relative number of undifferentiated cells in a cell population including haematopoietic cells, which device comprises

a chamber, means for introducing into said chamber a cell population including haematopoietic cells, means for introducing into said chamber an agent capable of increasing the relative number of undifferentiated cells in a cell population, incubation means for incubating said committed cells in the presence of said agent, and mixing means for mixing the agent and the cell population in the chamber.

41. (Previously presented) A device for forming and/or increasing the relative number of cells having a cell surface marker designation CD34+ and/or HLA-DR- and/or CD38- and/or CD117 and/or AC133 and/or CD90 and/or CD45low in a cell population including committed cells, which device comprises a chamber, means for introducing into said chamber a cell population including committed cells, means for introducing into said chamber an agent that operably engages said committed cells, and incubation means operable to incubate said committed cells that are engaged by said agent in said chamber such that the relative number of CD34+ and/or HLA-DR- and/or CD38- and/or CD117 and/or AC133 and/or CD90 and/or CD45low cells increases as a result of said engaging, and mixing means for mixing the agent and the cell population in the chamber.

42. (Withdrawn) A method of preparing an undifferentiated cell, the method comprising retrodifferentiating a more committed cell to an undifferentiated cell, wherein the retrodifferentiation of the more committed cell occurs to the more committed cell in or from a buffy coat blood sample.

43. (Withdrawn) A method of preparing an undifferentiated cell, the method comprising contacting a more committed cell in a buffy coat blood sample with an agent that causes the more committed cell to retrodifferentiate into an undifferentiated cell.

44. (Withdrawn) A method according to claims 42 or 43 wherein the committed cells are non-cancer cells.

45. (Withdrawn) A method according to any one of claims 42 or 43 wherein the committed cells are differentiated cells.

46. (Withdrawn) A method according to claim 44 wherein the committed cells are differentiated cells.

47. (Withdrawn) A method according to any one of claims 42 or 43 wherein the committed cells are committed haematopoietic cells.

48. (Withdrawn) A method according to claim 44 wherein the committed cells are committed haematopoietic cells.

49. (Withdrawn) A method according to any one of claims 42 or 43 wherein the committed cells are selected from CFC-T cells, CFC-B cells, CFC-Eosin cells, CFC-Bas cells, CFC-GM cells, CFC-MEG cells, CFC-E cells, T cells and B cells.

50. (Withdrawn) A method according to any one of claims 42 or 43 wherein the undifferentiated cells are pluripotent stem cells.

51. (Withdrawn) A method according to any one of claims 42 or 43 wherein the undifferentiated cells are stem cells selected from the group consisting of haematopoietic stem cells, neuronal stem cells, epithelial stem cells, mesenchymal stem cells and embryonic stem cells.

52. (Withdrawn) A method according to any one of claims 42 or 43 wherein the undifferentiated cells are characterised by one or more of the following cell surface marker designations: CD34+, HLA-DR-, CD38-, CD117, AC133, CD90 and/or CD45low.

53. (Withdrawn) A method according to any one of claims 42 or 43 wherein the undifferentiated cells are MHC class I+ and/or MHC class II+ cells.

54. (Withdrawn) A method according to any one of claims 42 or 43 wherein the agent engages a receptor that mediates capture, recognition or presentation of an antigen at the surface of the committed cells.

55. (Withdrawn) A method according to claim 54 wherein the receptor is an MHC class I antigen or an MHC class II antigen.

56. (Withdrawn) A method according to claim 55 wherein the class I antigen is an HLA-A receptor, an HLA-B receptor, an HLA-C receptor, an HLA-E receptor, an HLA-F receptor or an HLA-G receptor and said class II antigen is an HLA-DM receptor, an HLA-DP receptor, an HLA-DQ receptor or and HLA-DR receptor.

57. (Withdrawn) A method according to claim 56 wherein the receptor is an HLA-DR receptor.

58. (Withdrawn) A method according to claim 54 wherein the receptor comprises a  $\beta$ -chain having homologous regions.

59. (Withdrawn) A method according to claim 58 wherein the receptor comprises at least the homologous regions of the  $\beta$ -chain of HLA-DR.

60. (Withdrawn) A method according to claim 54 wherein the agent is an antibody to the receptor.

61. (Withdrawn) A method according to claim 60 wherein the agent is a monoclonal antibody to the receptor.

62. (Withdrawn) A method according to claim 61 wherein the antibody is selected from the group consisting of monoclonal antibody CR3/43 and the monoclonal antibody TAL 1B5.

63. (Withdrawn) A method according to any one of claims 42 or 43 wherein the agent modulates MHC gene expression.

64. (Withdrawn) A method according to claim 63 wherein the agent modulates MHC class I+ and/or MHC class II+ expression.

65. (Withdrawn) A method of increasing the relative number of cells having a cell surface marker designation CD34+ and/or HLA-DR- and/or CD38- and/or CD117 and/or AC133 and/or CD90 and/or CD45<sup>low</sup> in a buffy coat blood sample, the method comprising contacting a more committed cell in a buffy coat blood sample with an agent that operably engages said committed cells, such that the relative number of CD34+ and/or HLA-DR- and/or CD38- and/or CD117 and/or AC133 and/or CD90 and/or CD45<sup>low</sup> cells increases as a result of said engaging.

66. (Withdrawn) A method of preparing an undifferentiated cell, the method comprising contacting one or more differentiated cells in a cell population with retrodifferentiation means effective to displace the ratio of normal differentiated cells in said population, whereby one or more of said differentiated cells is caused to retrodifferentiate to an undifferentiated cell(s).

67. (Withdrawn) A method of using retrodifferentiating means to displace the ratio of normal differentiated cells in a cell population to effect retrodifferentiation of one or more of said differentiated cells to an undifferentiated cell(s).

68. (Withdrawn) A method of preparing an undifferentiated cell, the method comprising retrodifferentiating a differentiated cell in a cell population to an undifferentiated cell, wherein the environment comprising said cell population comprising one or more differentiated cells is changed from a first environment to a second environment wherein the free ion concentration of said second environment is effectively modified as compared with the first environment so as to cause one or more of said differentiated cells to retrodifferentiate to an undifferentiated cell(s).

69. (Withdrawn) A method of preparing an undifferentiated cell, the method comprising contacting one or more differentiated cells in a cell population with retrodifferentiation means

effective to displace the ratio of normal differentiated cells, culturing the cell population in a ion free or ion sequestered first environment, and changing the first environment to a second environment wherein the concentration of ions present in the second environment is effectively modified as compared with the first environment, thus to effect one or more of the differentiated cells to retrodifferentiate to an undifferentiated cell(s).

70. (Withdrawn) A method according to any one of claims 66-67 or 69 wherein said retrodifferentiating means is any means which causes negative selection within the cell population and thus causes a disruption of the ratio of normal differentiated cells in a cell population.

71. (Withdrawn) A method according to any one of claims 66-67 or 69 wherein said retrodifferentiating means is any one or more of the following: an antibody; a density gradient medium used to separate cells according to the density of the cells; or a substance which causes sedimentation of red blood cells.

72. (Withdrawn) A method according to claim 68 or 69 wherein the free ion concentration of said second environment is increased compared with that of the first environment.

73. (Withdrawn) A method according to any one of claims 68 or 69 wherein the relative free ion concentration of second environment is increased compared with the first environment.

74. (Withdrawn) A method according to any one of claims 68 wherein the free ion is an anion.

75. (Withdrawn) A method according to any one of claims 68 wherein the free ion is a group I or group II metal.

76. (Withdrawn) A method according to any one of claims 68 wherein the free ion is a calcium ion and/or a magnesium ion.

77. (Withdrawn) A method according to any one of claims 68 or 69 wherein the ion concentration is modified by treating said first environment with an agent capable of relatively changing the free ion concentration of the environment to effect said second environment.

78. (Withdrawn) A method according to claim 77 wherein said first environment is treated with one or more ion sequestering agents, which is subsequently removed or reduced in concentration, thus to effect a second environment having a relatively increased free ion



concentration, thus effecting retrodifferentiation of one or more differentiated cells in the cell population.

79. (Withdrawn) A method according to any one of claims 68 or 69 wherein said first environment is treated with one or more free ion sequestering agents and the cell population is subsequently transferred to a second environment, which second environment has an increased free ion concentration as compared with the first environment, thus effecting retrodifferentiation of the one or more differentiated cells in the cell population.

80. (Withdrawn) A method according to any one of claims 68 or 69 wherein said cell population may be cultured in a first environment comprising a low or zero concentration of free ions followed by transferring the cell population to or adjusting the first environment so that it becomes a second environment comprising free ions or comprising free ions at a higher concentration than the first environment, thus effecting retrodifferentiation of one or more differentiated cells in the cell population.

81. (Withdrawn) A method according to claim 78 wherein said sequestering agent is a free ion chelating agent.

82. (Withdrawn) A method according to claim 81 wherein said sequestering agent comprises both an amine and a carboxylic group.

83. (Withdrawn) A method according to claim 82 wherein said sequestering agent comprises a plurality of  $-N(CH_2CO_2H)_n$  groups, wherein  $n=1$  or  $n=2$ .

84. (Withdrawn) A method according to claim 78 wherein said sequestering agent comprises any one or more of the following: EDTA, heparin, EGTA, DTPA, trisodium citrate and other similar chelating agents and/or anticoagulants.

85. (Withdrawn) A method according to claim 78 wherein said sequestering agent is added in a sufficiently high concentration such that removal of the presence of said sequestering agent causes retrodifferentiation.

86. (Withdrawn) A method according to claim 85 wherein said concentration of the sequestering agent sufficient to cause retrodifferentiation when the presence of thereof is removed is more than or equal to about 2mM.

87. (Withdrawn) A method according to any one of claims 66-69 wherein the differentiated cells are non-cancer cells.

88. (Withdrawn) A method according to any one of claims 66-69 wherein the differentiated cells are committed haematopoietic cells.

89. (Withdrawn) A method according to any one of claims 66-69 wherein the differentiated cells are selected from CFC-T cells, CFC-B cells, CFC-Eosin cells, CFC-Bas cells, CFC-GM cells, CFC-MEG cells, CFC-E cells, T cells and B cells.

90. (Withdrawn) A method according to any one of claims 66-69 wherein the undifferentiated cells are pluripotent stem cells.

91. (Withdrawn) A method according to any one of claims 66-69 wherein the undifferentiated cells are stem cells from the group consisting of haematopoietic stem cells, neuronal stem cells, epithelial stem cells, mesenchymal stem cells, endodermal stem cells and embryonic stem cells.

92. (Withdrawn) A method according to any one of claims 66-69 wherein the undifferentiated cells are characterised by one or more of the following cell surface marker designations: CD34+, HLA-DR-, CD38-, CD117, AC133, CD90 and/or CD45low.

93. (Withdrawn) A method according to any one of claims 66-69 wherein the undifferentiated cells are MHC class I+ and/or MHC class II+ cells.

94. (Withdrawn) A method according to any one of claims 66-69 wherein the cell population including committed cells is a buffy coat blood sample or is from a buffy coat blood sample.

95. (Withdrawn) A method of preparing an undifferentiated cell, the method comprising retrodifferentiating a differentiated cell in a cell population to an undifferentiated cell, wherein the environment comprising said cell population comprising one or more differentiated cells is changed from a first environment having a low or zero concentration of free calcium or magnesium ions to a second environment comprising free calcium or magnesium ions or comprising free calcium or magnesium ions at a higher concentration than the first environment, thus effecting retrodifferentiation of one or more differentiated cells in the cell population.

96. (Withdrawn) A method of preparing an undifferentiated cell, the method comprising retrodifferentiating a differentiated haematopoietic cell in a cell population to an undifferentiated cell, wherein the environment comprising said cell population comprising one or more differentiated haematopoietic cells is changed from a first environment to a second environment wherein the free ion concentration of said second environment is effectively modified as

compared with the first environment so as to cause one or more of said differentiated haematopoietic cells to retrodifferentiate to an undifferentiated cell(s).

97. (Withdrawn) A method of preparing an undifferentiated cell, the method comprising retrodifferentiating a differentiated cell in a cell population to an undifferentiated cell, wherein the environment comprising said cell population is modified by treating a first environment with an agent capable of relatively changing the free ion concentration of the environment to effect a second environment.

98. (Withdrawn) A business method comprising supplying a device as claimed in any one of claims 1-4 and/or means that are capable of causing a committed cell to retrodifferentiate into an undifferentiated cell and/or an agent that causes a committed cell to retrodifferentiate into an undifferentiated cell.

99. (Withdrawn) The method of claim 98 comprising supplying means that are capable of causing a committed cell to retrodifferentiate into an undifferentiated cell and/or an agent that causes a committed cell to retrodifferentiate into an undifferentiated cell in response to an order therefor placed by a device that employs such means and/or agent.

100. (Withdrawn) A business method comprising receiving communications from a device as claimed in any one of claims 3, 4, 17 or 18 and responding thereto by filling orders and/or confirming that operations are being or have been performed correctly and/or providing instructions as to operations.

101. (Currently amended) A device for treating a starting hematopoietic cell population comprising committed cells with an agent capable of increasing the relative number of undifferentiated cells, which device comprises:

(a) a [[first]] support hook for attachment of [[a]] an inlet storage container containing a starting cell population, wherein said inlet storage container is a blood bag.

(b) a heated incubation chamber,

(c) means for drawing the starting cell population from the inlet storage container into the heated incubation chamber,

(d) a refrigerated chamber for insertion of a syringe containing the agent,

(e) means for delivering the agent from the refrigerated chamber into the heated incubation chamber,

(f) means for mixing the agent and the cell population in the heated incubation chamber,

(g) a ~~second support hook for attachment of~~ means for hanging an outlet storage container, wherein said outlet storage container is a blood bag, and

(h) means for drawing the treated cell population from the heated incubation chamber into the outlet storage container.

102-103. (Canceled)

104. (Previously presented) A device according to claim 101 wherein the means for drawing the starting cell population from the inlet storage container into the heated incubation chamber comprises a peristaltic pump.

105. (Previously presented) A device according to claim 101 wherein the means for drawing the treated cell population from the incubation chamber into the outlet storage container comprises a peristaltic pump.

106. (Currently amended) A device according to claim 101 wherein the [[first]] support hook forms part of an electronic balance for weighing the inlet storage container.

107. (Previously presented) The device according to claim 101 wherein the means for delivering the agent from the refrigerated chamber into the heated incubation chamber comprises a stepper motor for discharging a syringe.